REMARKS

In the Final Action dated April 29, 2010, claims 1, 7-10 and 13-30 were pending, of which claims 13-29 were withdrawn from further consideration as drawn to non-elected inventions.

The previous rejection under 35 U.S.C. §103(a) based on Morin et al. (*Clinical & Experimental Immunology* 134(3): 388-395, 2003), applied to claims 1, 3 and 5-10, has been withdrawn in view of Applicant's amendments and remarks submitted on March 15, 2010. However, the Examiner has now rejected claims 1, 7-10 and 30 under 35 U.S.C. §103(a) as allegedly obvious over Maraskovsky et al. (*J. Exp. Med.* 1996; 184: 1953-1962) in view of Morel et al. (*Clin. Exp. Immunol.* June 23, 2003; 133(1): 1-10).

Specifically, the Examiner contends that Maraskovsky teaches "*in vivo* administration of Flt3L results in a dramatic numerical increase of DC in multiple tissues in mice" and further indicates that a subpopulation of these dendritic cells expresses CD8a. Maraskovsky also allegedly teaches that dendritic cells induce immune tolerance and is promising for immunotherapy.

The Examiner admits that Maraskovsky does not teach the relevance of an increased subpopulation of $CD8^+$ dendritic cells to inducing immune tolerance for delaying the onset of diabetes. However, the Examiner attempts to rely on Morel to cure this deficiency of Maraskovsky. The Examiner alleges that Morel teaches the therapeutic effect of distinct DC subsets on autoimmune disease (referring to Table 2 of Morel), and induction of immune tolerance in mice by CD8a+ dendritic cells (referring to page 2, col. 1., lines 23-25 of Morel). Morel also allegedly teaches that increased numbers of DC cells were related to increased levels of Flt-3L (page 4, col.2). Therefore, the Examiner contends that it would have been obvious to

the person of ordinary skill in the art, at the time of the invention was made, to combine the teachings of Maraskovsky and Morel and administer Flt-3L to a subject to delay onset of diabetes.

Applicants respectfully disagree.

As presently recited, claim 1 is directed to a method for delaying onset of diabetes in a subject comprising administering to said subject Flt-3L, wherein Flt-3L is administered to said subject as the sole active component in an amount effective to increase a sub-type of non-activated, immature and tolerogenic DC selected from Plasmacytoid DC, $CD8^+$ DC or their equivalents, thereby inducing or maintaining immune tolerance in said subject which delays onset of diabetes.

Applicants respectfully submit that the Examiner's characterization of Morel's teachings is inaccurate. The Examiner refers to Table 2 of Morel for teachings of a therapeutic effect of CD8a+ DC. In fact, Table 2 indicates that the DCs which can prevent diabetes are myeloid CD8a- (i.e., CD8a negative, not CD8a positive; column 1 of Table 2). In the same table, Morel refers to Clare-Salzer (*J. Clin. Invest.* 1992; 90: 741-748) and Naumov (*Proc. Natl. Acad. Sci. U.S.A.* 2001 Nov 20; 98(24):13838-43) in support of the role of CD8a- DCs in preventing diabetes. Applicants have provided copies of these two references, and direct the Examiner's attention to Naumov (2001), page 13842, right column, second paragraph from the bottom.

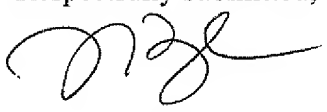
Further, Morel teaches that the DCs which may have a therapeutic role in prevention of diabetes in NOD mice are mature BM-derived DC (see page 5, column 1, paragraph entitled "Autoimmune (type-1) diabetes", lines 10-12), rather than the immature cells, as recited in the

instant claim 1. Furthermore, Table 2 of Morel also indicates that CD8a- and *mature* myeloid DCs are responsible for the therapeutic effects observed in NOD mouse.

Therefore, it is respectfully submitted that Morel teaches away from the invention by disclosing that CD8- mature DCs prevent diabetes. Therefore, those skilled in the art would not have combined Maraskovsky with Morel to administer Flt3 ligand *in vivo* to in order to delay the onset of diabetes, as presently claimed in claim 1. As such, the method of claim 1 and its dependent claims (claims 7-10 and 30) are not obvious over the combination of Maraskovsky and Morel. Withdrawal of the rejection under 35 U.S.C. §103(a) is therefore respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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Enc.: Clare-Salzer (1992) and Naumov (2001).